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in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress
(FEDRIP) now available
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results now available
NEWS 10 Jun 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFULL has been reloaded
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NEWS 17 Aug 08
PHARMAMarketLetter(PHARMAML) - new on STN
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enhanced
NEWS 23 Sep 03 JAPIO has been reloaded and
enhanced
NEWS 24 Sep 16 Experimental properties added to
the REGISTRY file
NEWS 25 Sep 16 Indexing added to some pre-1967
records in CAVCAPLUS
NEWS 26 Sep 16 CA Section Thesaurus available in
CAPLUS and CA
NEWS 27 Oct 01 CASREACT Enriched with
Reactions from 1907 to 1985
NEWS 28 Oct 21 EVENTLINE has been reloaded
NEWS 29 Oct 24 BEILSTEIN adds new search fields
NEWS 30 Oct 24 Nutraceuticals International
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NEWS 31 Oct 25 MEDLINE SDI run of October 8,
2002

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APOLLIT

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to REGISTRY

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NEWS 35 Dec 04 CSA files on STN

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V6.0a(ENG) AND V6.0Ja(JP),

AND CURRENT DISCOVER FILE IS DATED

01 OCTOBER 2002

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***** STN Columbus *****

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CHEMICAL SOCIETY (ACS)

FILE 'BIOTECHNO' ENTERED AT 10:13:16 ON 04
DEC 2002
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=> s (interleukin-11 or il-11 or interleukin11 or il11)
L1 8306 (INTERLEUKIN-11 OR IL-11 OR
INTERLEUKIN11 OR IL11)

=> s l1 (P) (inflamm? or mucositis)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT
WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7 (P)'
L2 1178 L1 (P) (INFLAMM? OR MUCOSITIS)

=> s l2 (p) (treat? or administ? or therap? or method?)
3 FILES SEARCHED...
4 FILES SEARCHED...
5 FILES SEARCHED...
PROXIMITY OPERATOR LEVEL NOT CONSISTENT
WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L15 (P)'
L3 682 L2 (P) (TREAT? OR ADMINIST? OR
THERAP? OR METHOD?)

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS,
EMBASE, CANCERLIT, BIOSIS, USPATFULL,
BIOTECHNO'
KEEP DUPLICATES FROM MORE THAN ONE FILE?
Y/(N):n
PROCESSING COMPLETED FOR L3
L4 299 DUPLICATE REMOVE L3 (383
DUPLICATES REMOVED)

=> s l1 (p) (mucositis)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT
WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7 (P)'
L5 79 L1 (P) (MUCOSITIS)

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS,
EMBASE, CANCERLIT, BIOSIS, USPATFULL,
BIOTECHNO'
KEEP DUPLICATES FROM MORE THAN ONE FILE?
Y/(N):n
PROCESSING COMPLETED FOR L5
L6 27 DUPLICATE REMOVE L5 (52
DUPLICATES REMOVED)

=> d l5 1- ibib, abs
YOU HAVE REQUESTED DATA FROM 79 ANSWERS
- CONTINUE? Y/(N):n

=> d l6 1- ibib, abs

YOU HAVE REQUESTED DATA FROM 27 ANSWERS
- CONTINUE? Y/(N):y

L6 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2002
ACS
ACCESSION NUMBER: 2002:220397 CAPLUS
DOCUMENT NUMBER: 136:252503
TITLE: Topical formulations for delivery of
interleukin-11
INVENTOR(S): Warne, Nicholas W.; Bedrosian,
Camille L.; Keith,
James C., Jr.; Schwerschlag, Ullrich S.;
Schendel,
Paul F.
PATENT ASSIGNEE(S): Genetics Institute, Inc.,
USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.
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WO 2002022156	A2	20020321	WO 2001-US28886 20010917
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WO 2002022156	A3	20020613	
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		

RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
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AU 2001089102	A5	20020326	AU 2001-89102 20010917
PRIORITY APPLN. INFO.:			US 2000-662994 A1 20000915

WO 2001-US28886 W 20010917			
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AB Topical formulations of interleukin-11 are disclosed for treating a variety of disorders, including inflammatory bowel diseases (e.g., Crohn's disease, ulcerative colitis, indeterminate colitis, and infectious colitis), mucositis (e.g., oral mucositis, gastrointestinal mucositis, nasal mucositis, and proctitis), necrotizing enterocolitis, inflammatory skin disorders (e.g., psoriasis, atopic dermatitis, and contact hypersensitivity), aphthous ulcers, pharyngitis, esophagitis, peptic ulcers, gingivitis, periodontitis, and ocular diseases (e.g., conjunctivitis, retinitis, and uveitis). Multiparticulate formulations of rhIL-11, in which rh

IL-11 was sprayed onto a sucrose bead and covered with a sealant and an enteric coating were prepd. (1 mg active ingredient/100 mg multiparticulates) and tested in the neutropenic rat model. Orally administered rhIL-11 provides mucosal protection against chemotherapy-induced mucosal injury and maintains gut barrier function in exptl. animal models. Levels of circulating endotoxin were significantly reduced in the rhIL-11 treated rats (0.4 ng/mL) compared to the control treated rats (4.04 ng/mL) and the quant. microbiol. for *P. aeruginosa* in liver and spleen tissue was significantly reduced in the rhIL-11 treated rats compared to the control rats.

L6 ANSWER 2 OF 27 USPATFULL

ACCESSION NUMBER: 2002:109176

USPATFULL

TITLE: Human 2-19 protein homologue, z219a

INVENTOR(S): Conklin, Darrell C., Seattle, WA, United States

Blumberg, Hal, Seattle, WA, United States

PATENT ASSIGNEE(S): ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)

NUMBER	KIND	DATE
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PATENT INFORMATION:	US 6388064	B1
20020514		
APPLICATION INFO.:	US 1998-167513	
19981006 (9)		

NUMBER	DATE
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PRIORITY INFORMATION:	US 1997-61712P
19971006 (60)	

DOCUMENT TYPE: Utility

FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Eyler, Yvonne

ASSISTANT EXAMINER: Lazar-Wesley, Eliane

LEGAL REPRESENTATIVE: Johnson, Jennifer K.

NUMBER OF CLAIMS: 6

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 3127

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to polynucleotide and polypeptide molecules for z219a, a novel member of the human 2-19 protein family.

The polypeptides, and polynucleotides encoding them, may be used for detecting human chromosomal abnormalities. The present invention also includes antibodies to the z219a polypeptides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:862621 CAPLUS

TITLE: Effect of Interleukin-11 on Ameliorating Intestinal Damage After Methotrexate Treatment of Breast Cancer in Rats

AUTHOR(S): Gibson, Rachel J.; Keefe, Dorothy M. K.; Thompson, Fiona M.; Clarke, Julie M.; Goland, Gary J.; Cummins, Adrian G.

CORPORATE SOURCE: Department of Medical Oncology, The Royal Adelaide Hospital, Adelaide

SOURCE: Digestive Diseases and Sciences (2002), 47(12),

2751-2757

CODEN: DDSCDJ; ISSN: 0163-2116

PUBLISHER: Kluwer Academic/Plenum Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Gastrointestinal mucositis after cancer

chemotherapy is an

increasing problem that is essentially untreatable once established,

although it gradually remits. The aim of this study was to investigate

the time-course and effect of interleukin-11 (IL-11) on apoptosis and intestinal morphometry as measures of mucositis. Female DA rats were

implanted s.c. with

syngeneic breast cancer and treated with methotrexate (MTX). Intestinal

morphometry was used to assess villus area, crypt length, and mitotic

count per crypt. Apoptosis was assessed by TUNEL assay in the tumor and

jejunum. Tumor proliferation was assessed by mitotic count. The

time-course study showed that MTX increased apoptosis by 28-fold in the

crypts of the small intestine and by 3-fold in the tumor, and peaked at 6

h after chemotherapy. IL-11 (100 .mu.g/kg/ twice daily s.c.) maintained intestinal wt., and reduced the severity of

mucositis, as measured by villus area, crypt length, and mitotic

count per crypt. IL-11 at higher doses (200 .mu.g and

400 .mu.g/kg/twice daily s.c.), did not further improve villus area, crypt

length, and mitotic count per crypt. IL-11 did not affect tumor apoptosis or proliferation. We conclude that IL-

11 attenuated mucositis by maintaining intestinal wt. and morphometry. IL-11 did not prevent apoptosis,

but

rather induced compensatory crypt cell proliferation.

L6 ANSWER 4 OF 27 MEDLINE

DUPLICATE 1

ACCESSION NUMBER: 2002192086 IN-PROCESS

DOCUMENT NUMBER: 21916472 PubMed ID: 11919725

TITLE: A phase I/II double-blind, placebo-controlled study of recombinant human interleukin-11 for

mucositis and acute GVHD prevention in allogeneic stem cell transplantation.

AUTHOR: Antin J H; Lee S J; Neuberg D; Alyea E; Soiffer R J; Sonis S; Ferrara J L M

CORPORATE SOURCE: Department of Adult Oncology and Biostatistical Science, Dana-Farber Cancer Institute, Boston, MA 02115, USA.

SOURCE: BONE MARROW TRANSPLANTATION, (2002 Mar) 29 (5) 373-7. Journal code: 8702459. ISSN: 0268-3369.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20020403
Last Updated on STN: 20020403

AB Interleukin-11 (IL-11) decreases cytokine release and increases survival in murine BMT models. In these systems, it reduces gut permeability, partially polarizes T cells to a Th2 phenotype, down-regulates IL-12, prevents mucositis, and accelerates recovery of oral and bowel mucosa. We conducted a randomized double-blind pilot study of rhIL-11 administered with cyclosporine/MTX prophylaxis after cytotoxic/TBI conditioning and allogeneic stem cell transplantation for hematologic malignancies. Patients received rhIL-11, 50 microg/kg subcutaneously daily or placebo in a 3:1 ratio. Treatment was administered prior to the start of conditioning and continued up to 21 days. The study was designed to assess safety with stopping rules for cardiac arrhythmias and mortality. Although projected to accrue 20 patients, only 13 patients (10 IL-11, three placebo) were enrolled because the early stopping rule for mortality was triggered. Of 10 evaluable patients who received IL-11, four died by day 40 and one died on day 85. Deaths were attributable to transplant-related toxicity. One of three placebo recipients died of suicide, the other two are alive. Patients receiving IL-11 had severe fluid retention and early mortality, making it impossible to determine whether IL-11 given in this schedule can reduce the rate of GVHD. Grade B-D acute GVHD occurred in two of eight evaluable patients on IL-11 and one of three patients on placebo. The primary adverse events of the study were severe fluid retention resistant to diuresis (average weight gain 9 +/- 4%) and multiorgan failure in five of 10 evaluable patients. The use of IL-11 as GVHD prophylaxis in allogeneic transplantation cannot be recommended as administered in this trial.

L6 ANSWER 5 OF 27 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 2002159106 MEDLINE
DOCUMENT NUMBER: 21887199 PubMed ID: 11890354

TITLE: Oprelvekin. Genetics Institute.

AUTHOR: Sitaraman S V; Gewirtz A T

CORPORATE SOURCE: Emory University School of Medicine, Department of Pathology and Laboratory Medicine, Atlanta, GA 30322, USA..
ssitar2@emory.edu

SOURCE: Curr Opin Investig Drugs, (2001 Oct) 2 (10) 1395-400. Ref: 34
Journal code: 100965718. ISSN: 1472-4472.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW) (REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200210

ENTRY DATE: Entered STN: 20020314
Last Updated on STN: 20021031
Entered Medline: 20021030

AB Genetics Institute has developed and launched oprelvekin (rhIL-11; Neumega), a recombinant form of human IL-11. In November 1997, the FDA cleared oprelvekin for the prevention of severe thrombocytopenia and the reduction of the need for platelet transfusions following myelosuppressive chemotherapy in susceptible patients with non-myeloid malignancies 12703021. The product was launched at the end of 1997 [312556]. By December 1999, phase III trials for Crohn's disease (CD) were underway [363007]. Genetics Institute had commenced a 150-patient phase II trial for mild-to-moderate CD and mucositis and the company planned to file regulatory procedures for the indication of CD in 1999 [271210]. An oral formulation for this indication has been developed. Oprelvekin is also undergoing phase I clinical trials for colitis [396157], phase II clinical trials for rheumatoid arthritis [413835] and clinical trials for psoriasis [299644]. In March 1997, Wyeth-Ayerst became the licensee for Europe, Africa, Latin America and Asia (with the exception of Japan). Genetics Institute holds marketing rights for North America [239273]. In Japan, oprelvekin is being developed by Genetics Institute and Yamanouchi; phase III trials have commenced [295049] and were ongoing in May 2001 [411763]. In April 1996, analysts at Yamaichi estimated launch in 2001 and maximum annual sales of over yen 10 billion [215896]. In January 1998, Morgan Stanley Dean Witter predicted

Yamanouchi's share of sales to be yen 1 billion in 2001, rising to yen 2 billion in 2002 [315458]. Sales of oprelvekin were US \$34 million for Genetics institute in fiscal 2000 while, in July 2001, Credit Suisse First Boston estimated that this figure will be US \$30 million and US \$34 million in 2001 and 2002, respectively [416883].

L6 ANSWER 6 OF 27 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002101064 EMBASE
TITLE: Mucosal barrier injury (MBI) after intensive chemotherapy.
AUTHOR: Cioch M.
CORPORATE SOURCE: Dr. M. Cioch, Klinika Hematoonkologii, Transplantacji Szpiku, ul. Jaczewskiego 8, 20-954 Lublin, Poland.
hematol@free.med.pl
SOURCE: Onkologia Polska, (2001) 4/2 (85-89).

Refs: 33
ISSN: 1505-6732 CODEN: OPNOAS
COUNTRY: Poland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mucosal barrier injury (MBI) is reported to affect 60% to 100% of bone marrow transplant recipients. Oral and gut mucositis may manifest not only locally but also by severe generalised syndromes. MBI consists of 4 phases: inflammatory, epithelial, ulcerative-bacteriological and healing. Modern treatment consists of amifostine, glutamine, GM-CSF, antibiotics, antifungal drugs and parenteral nutrition agents. Future directions are the following: IgA-IgG administered orally, KGF, EGF, TGF, IL-11, MAD-11.

L6 ANSWER 7 OF 27 MEDLINE
DUPLICATE 3
ACCESSION NUMBER: 2001641774 MEDLINE
DOCUMENT NUMBER: 21551334 PubMed ID: 11694562
TITLE: Inflammatory cytokines and mucosal injury.
AUTHOR: Williams D A
CORPORATE SOURCE: Howard Hughes Medical Institute, Indiana University School of Medicine, Department of Pediatrics, Indianapolis, USA.
dwilliam@iupui.edu
SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE. MONOGRAPHS, (2001) (29) 26-30. Ref: 51
Journal code: 9011255. ISSN: 1052-6773.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020125
Entered Medline: 20020114
AB The cause of mucosal injury in inflammatory bowel disease (IBD) is not clear but likely involves infectious agents or other toxins followed by an abnormal immune response in genetically susceptible individuals. The inflammatory cytokines appear to play a key role in both the susceptibility of some individuals and the tissue damage that accompanies IBD. The generation of transgenic and gene-targeted (knockout) animals has provided invaluable information regarding the cytokines and cellular immune effectors that are important in IBD. Information from these and other preclinical animal models, such as those involving interleukin 11, has led to human trials testing novel therapies for IBD and other diseases in which inflammation of the gut mucosa is an important component. Thus, expression of inflammatory cytokines appears to be an important target for the development of novel therapies for IBD and other diseases in which intestinal mucosal damage occurs, such as mucositis and graft-versus-host disease.

L6 ANSWER 8 OF 27 MEDLINE
DUPLICATE 4
ACCESSION NUMBER: 2001641772 MEDLINE
DOCUMENT NUMBER: 21551332 PubMed ID: 11694560
TITLE: Protection against mucosal injury by growth factors and cytokines.
AUTHOR: Booth D; Potten C S
CORPORATE SOURCE: Cancer Research Campaign Epithelial Biology Group, Paterson Institute for Cancer Research, Christie Hospital, Manchester, UK.
SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE. MONOGRAPHS, (2001) (29) 16-20. Ref: 20
Journal code: 9011255. ISSN: 1052-6773.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020125
Entered Medline: 20020114
AB This article provides an overview of published studies in which growth factors and cytokines were used to modify the sensitivity of intestinal

stem cells to a dose of radiation. In these experiments, growth factors were used to manipulate the sensitivity of stem cells in the gastrointestinal tract to reduce the severity of gastrointestinal mucositis in cancer therapy patients. Transforming growth factor beta3, interleukin 11, and keratinocyte growth factor were used. All three agents, given according to appropriate protocols, can result in a threefold to fourfold increase in the number of intestinal stem cells that survive a dose of radiation therapy. This result was assessed by using the crypt microcolony assay of stem cell functional capacity. The changes in stem cell survival that were observed resulted in increased animal survival. This increased survival was taken as a surrogate for improvement in patient well-being. The severity of diarrhea, a marker of functional impairment, was concomitantly reduced.

L6 ANSWER 9 OF 27 MEDLINE
 DUPLICATE 5
 ACCESSION NUMBER: 2001377270 MEDLINE
 DOCUMENT NUMBER: 21328732 PubMed ID:
 11436115
 TITLE: Mucositis associated with stem cell
 transplantation:
 current status and innovative approaches
 to management.
 AUTHOR: Stiff P
 CORPORATE SOURCE: Loyola University Medical
 Center, 2160 South First Avenue,
 Maywood, IL 60153, USA.
 SOURCE: BONE MARROW
 TRANSPLANTATION, (2001 May) 27 Suppl 2 S3-S11.
 Ref: 64
 Journal code: 8702459. ISSN: 0268-3369.
 PUB. COUNTRY: England: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL
 ARTICLE)

General Review; (REVIEW)
 (REVIEW, TUTORIAL)

LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200110
 ENTRY DATE: Entered STN: 20011015
 Last Updated on STN: 20011015
 Entered Medline: 20011011
 AB Treatment-related morbidity, and in some cases, mortality, associated with autologous and allogeneic bone marrow transplantation has decreased in the past decade largely due to the use of blood stem cells combined with hematopoietic growth factors. However, these procedures remain morbid, with several series documenting regimen-related injury to the oral mucous membranes, the worst form of toxicity from a patient perspective. The pathophysiology of transplant-related mucositis is related to two major events: direct mucosal basal cell injury leading to atrophy and

ulcerations, and local infections that can become systemic, the latter of which are exacerbated by the severe neutropenia accompanying high-dose chemotherapy. Recent investigational agents designed to interfere with these two aspects of mucositis have been developed and are showing promise in early clinical trials. In particular, keratinocyte growth factor (KGF) and interleukin-11 appear active. They increase basal cell proliferation, prevent apoptosis due to the preparative regimen, and appear to ameliorate the mucositis seen with high-dose chemotherapy regimens. Oral, nonabsorbable anti-infective agents are also being tested in an attempt to prevent both local and systemic infections. Devoid of significant side-effects, KGF is now in large phase 2 trials that, if positive, will be a significant advance in promoting less morbid transplants by reducing pain and the risk of secondary infections and thus may reduce supportive care costs.

L6 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2002
 ACS DUPLICATE 6
 ACCESSION NUMBER: 2000:699078 CAPLUS
 DOCUMENT NUMBER: 133:280574
 TITLE: Methods of treating inflammatory
 bowel diseases by
 administering IL-11
 INVENTOR(S): Warne, Nick W.; Bedrosian,
 Camille L.; Keith, James
 C., Jr.; Schwertschlag, Ullrich S.;
 Schendel, Paul F.
 PATENT ASSIGNEE(S): Genetics Institute, USA
 SOURCE: U.S., 10 pp., Cont.-in-part of U.S.
 5,948,402.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO. NO. DATE	KIND	DATE	APPLICATION
US 6126933	A	20001003	US 1998-
179026 19981026			
US 5679339	A	19971021	US 1995-
495724 19950627			
WO 9701353	A1	19970116	WO 1996-
US8059 19960530			
W: AU, CA, JP, US			
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
US 5948402	A	19990907	US 1997-
892407 19970715			
US 6270759	B1	20010807	US 1999-
337965 19990622			
PRIORITY APPLN. INFO.:			US 1995-495724
A3 19950627			
			WO 1996-US8059 W
19960530			

19970715

AB Provided by the present invention are topical formulations of

Interleukin-11 and methods for treating a variety of disorders, including inflammatory bowel diseases (e.g., Crohn's disease, ulcerative colitis, indeterminate colitis, and infectious colitis), mucositis (e.g., oral mucositis, gastrointestinal mucositis, nasal mucositis, and proctitis), necrotizing enterocolitis, inflammatory skin disorders (e.g., psoriasis, atopic dermatitis, and contact hypersensitivity), aphthous ulcers, pharyngitis, esophagitis, peptic ulcers, gingivitis, periodontitis, and ocular diseases (e.g., conjunctivitis, retinitis, and uveitis). The topical administration of IL-11 is preferable to systemic injections, esp. in concurrent systemic administration with

chemotherapeutic or radiotherapeutic agent for cancer.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:316803 BIOSIS

DOCUMENT NUMBER: PREV200100316803

TITLE: Preliminary results of a phase I/II double-blind,

placebo-controlled study of recombinant human

interleukin-11 (rhIL-11) for mucositis and GVHD prevention in

allogeneic transplantation.

AUTHOR(S): Antin, Joseph H. (1); Lee, Stephanie J. (1); Harkness,

Shannon (1); Alyea, Edwin (1); Soiffer, Robert J. (1);

Rimm, Ilonna J.; Ferrara, James

CORPORATE SOURCE: (1) Dana-Farber Cancer Institute, Boston, MA USA

SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp.

786a. print.

Meeting Info.: 42nd Annual Meeting of the American Society

of Hematology San Francisco, California, USA December

01-05, 2000 American Society of Hematology

. ISSN: 0006-4971.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

AB GVHD is a major limitation in the successful application of marrow

transplantation to hematologic diseases. It may be due in part to

conditioning-induced tissue damage, transmigration of LPS across damaged

gut mucosa, and dysregulation of inflammatory cytokines. IL-

11 decreases cytokine release and increases survival in murine BMT

models. It reduces gut permeability, polarizes T cells to Th2 phenotype, and down-regulates IL-12. In other murine models IL-11

prevents mucositis and accelerates recovery of oral and bowel

mucosa. rhIL-11 also is used for the prevention of severe thrombocytopenia

after chemotherapy. To determine whether these effects would improve

outcome after human transplantation, we conducted a randomized

double-blind pilot study of rhIL-11 administered with standard

cyclosporine/MTX prophylaxis after cytoxan/TBI conditioning for

hematologic malignancies. Patients were

randomized to rhIL-11 50mg/kg sc

qd or placebo in a 3:1 ratio. Treatment was given within 24 hr of the

start of conditioning and continued for at most 21 d. Patient age 19-58

yr, 10 matched sib and 3 unrelated donor, 7 CML, 4 MDS 1 AML, 1 NHL. 10

received rhIL-11 and 3 received placebo. The study was designed to assess

safety with stopping rules for arrhythmias and mortality within 40 d. of

the BMT. While projected to accrue 20 patients, only 13 patients were

enrolled because the early stopping rule was triggered. 1 patient was

taken off study after a single dose because of LFT changes and is

considered evaluable for safety but not efficacy. Of 10 patients receiving

rhIL-11 and evaluable for safety, 4 died by day 40 and 1 died on day 85.

Cause of death included sepsis (2), multiorgan failure (1), and alveolar

hemorrhage (2). 1/3 placebo recipients died of suicide, the other two are

alive. Grade II-IV acute GVHD occurred in 2/8 evaluable patients on

rhIL-11 and 1/3 patients on placebo. 2/4 evaluable patients on the rhIL-11

arm developed chronic GVHD. The primary adverse events of the study were

severe fluid retention resistant to diuresis and multiorgan failure in

5/10 evaluable patients. 1-year survival of patients on rhIL-11 is 44%.

Patients receiving rhIL-11 had immediate toxicity consisting of fluid

retention and early mortality, making it impossible to determine whether

rhIL-11 given in this schedule can reduce the rate of GVHD. The use of

rhIL-11 as GVHD prophylaxis in allogeneic transplantation cannot be

recommended as administered in this trial.

L6 ANSWER 12 OF 27 MEDLINE

DUPLICATE 7

ACCESSION NUMBER: 2001045168 MEDLINE

DOCUMENT NUMBER: 20359857 PubMed ID: 10899677

TITLE: Defining mechanisms of action of interleukin-

11 on the progression of radiation-induced oral

mucositis in hamsters.

AUTHOR: Sonis S T; Peterson R L; Edwards L J; Lucey C A; Wang L;

Mason L; Login G; Ymamkawa M; Moses G; Bouchard P; Hayes L

L; Bedrosian C; Dorner A J

CORPORATE SOURCE: Division of Oral Medicine, Oral and Maxillofacial Surgery and Dentistry, Brigham and Women's Hospital, 75 Francis

Street, Boston, MA 02115, USA.

SOURCE: ORAL ONCOLOGY, (2000 Jul) 36 (4) 373-81.

Journal code: 9709118. ISSN: 1368-8375.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200012

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322

Entered Medline: 20001207

AB Oral ulcerative mucositis is a common toxicity associated with drug and radiation therapy for cancer. It impacts on quality of life and economic outcomes, as well as morbidity and mortality. Mucositis is often associated with dose limitations for chemotherapy or is a cause for dose interruption for radiation. The complexity of mucositis as a biological process has only been recently appreciated. It has been suggested that the condition represents a sequential interaction of oral mucosal cells and tissues, pro-inflammatory cytokines and local factors such as saliva and the oral microbiota. The recognition that the pathophysiology of mucositis is a multifactorial process was partially suggested by the observation that interleukin-11 (IL-11), a pleotropic cytokine, favorably altered the course of chemotherapy-induced mucositis in an animal model. In the current study, we evaluated a series of biologic and morphologic outcomes to determine their roles and sequence in the development of experimental radiation-induced mucositis and to evaluate the effects of IL-11 in attenuating them. Our results suggest that IL-11 favorably modulates acute radiation-induced mucositis by attenuating pro-inflammatory cytokine expression. Data are also presented which help define the pathobiological sequence of mucositis.

L6 ANSWER 13 OF 27 MEDLINE

DUPLICATE 8

ACCESSION NUMBER: 2000507405 MEDLINE

DOCUMENT NUMBER: 20508296 PubMed ID: 11053801

TITLE: Prevention and management of mucositis in patients with cancer.

AUTHOR: Herrstedt J

CORPORATE SOURCE: Department of Oncology 54 B1, Copenhagen University

Hospital, DK-2730 Herlev, Denmark..

jrhe@herlevhosp.kbhamt.dk

SOURCE: INTERNATIONAL JOURNAL OF ANTIMICROBIAL AGENTS, (2000 Oct)

16 (2) 161-3. Ref: 14

Journal code: 9111860. ISSN: 0924-8579.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200012

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322

Entered Medline: 20001220

AB This review summarises the large number of locally and systemically applied preventive and therapeutic interventions of mucositis in patients with cancer. The need for further elucidation of the pathophysiology and for optimisation of trial methodology is emphasised. Data from trials in animal models and preliminary data in patients indicate that cytokines such as interleukin-1, interleukin-11, TGF-beta 3 and keratinocyte growth factor could reduce the incidence of mucositis. Other potentially useful agents are the angiogenesis-inhibiting drug thalidomide, the cytoprotector amifostine and the pineal hormone melatonin.

L6 ANSWER 14 OF 27 MEDLINE

DUPLICATE 9

ACCESSION NUMBER: 1999287113 MEDLINE

DOCUMENT NUMBER: 99287113 PubMed ID: 10360368

TITLE: The biological basis for the attenuation of

mucositis: the example of interleukin-11.

AUTHOR: Sonis S; Edwards L; Lucey C

CORPORATE SOURCE: Division of Oral Medicine, Oral and Maxillofacial Surgery

and Dentistry, Brigham and Women's

Hospital, Boston, MA

02115, USA.

SOURCE: LEUKEMIA, (1999 Jun) 13 (6) 831-4.

Ref: 42

Journal code: 8704895. ISSN: 0887-6924.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199906

ENTRY DATE: Entered STN: 19990714

Last Updated on STN: 19990714

Entered Medline: 19990629

AB Oral mucositis is common, painful, dose-limiting toxicity of drug and radiation therapy for cancer. In granulocytopenic patients, the ulcerations which accompany mucositis are frequent portals of entry for indigenous oral bacteria often leading to bacteremias or sepsis.

The complexity of mucositis as a biological process has only recently been appreciated. The condition appears to represent a sequential interaction of the oral mucosal cells and tissues, pro-inflammatory cytokines, and local environmental factors in the mouth such as microorganisms and saliva. The recognition that the pathophysiology of mucositis is a multifactorial process has presented opportunities for intervention based on biological attenuation.

Interleukin-11, a pleiotropic cytokine, has a range of activities which is potentially relevant to mucositis. Consequently, it has been used successfully to modify the development, severity and course of mucositis in an animal model which closely mimics the equivalent human condition.

L6 ANSWER 15 OF 27 MEDLINE

DUPLICATE 10

ACCESSION NUMBER: 2000159268 MEDLINE

DOCUMENT NUMBER: 20159268 PubMed ID: 10694945

TITLE: Prevention and treatment of chemotherapy- and radiotherapy-induced oral mucositis: a review.

AUTHOR: Plevova P
CORPORATE SOURCE: Department of Radiotherapy, University Hospital of Ostrava, Ostrava-Poruba, Czech Republic..

pavlina.plevova@fnspo.cz
SOURCE: ORAL ONCOLOGY, (1999 Sep) 35 (5) 453-70. Ref: 225

Journal code: 9709118. ISSN: 1368-8375.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200003

ENTRY DATE: Entered STN: 20000327

Last Updated on STN: 20000327

Entered Medline: 20000316

AB Oral mucositis is a distressing toxic effect of systemic chemotherapy with many commonly utilized drugs and of head and neck irradiation in patients with cancer. The agents and methods that have been used and studied in chemotherapy- and radiotherapy-induced oral

mucositis, their mechanisms of action, and the current knowledge of their efficiency to reduce the incidence, severity or shorten the duration of oral mucositis are reviewed in this article.

Oral cooling is a cheap and available method to lower the severity of bolus 5-fluorouracil-induced oral mucositis. However, more effective

methods are needed. Results of studies with granulocyte-macrophage colony-stimulating factor or granulocyte colony-stimulating factor are promising. Lasers are partly beneficial, but equipment-demanding.

Modification of the chemotherapy regimen resulting in shortening of the exposition time to chemotherapy agents or chronomodulation of chemotherapy has been shown to lower mucosal toxicity of some regimens. Results of animal studies with locally applied transforming growth factor beta 3 and interleukin-11 are also promising. Based on the findings

of the role of the inflammatory cascade in the response of normal tissues to chemotherapy and radiotherapy, anti-inflammatory drugs might be beneficial. At the present time, no agent has been shown to be uniformly efficacious and can be accepted as standard therapy of chemotherapy- and radiotherapy-induced oral mucositis. Further intensive research is needed.

L6 ANSWER 16 OF 27 MEDLINE

DUPLICATE 11

ACCESSION NUMBER: 2000500979 MEDLINE

DOCUMENT NUMBER: 20499948 PubMed ID: 11045187

TITLE: [New cytokines and their role in supportive care].

Nove cytokiny a jejich mozne uplatneni v podperne lecbе.

AUTHOR: Klener P; Trnecny M
CORPORATE SOURCE: 1. interni klinika 1. lekarske fakulty a VFN Praha.

SOURCE: VNITRNI LEKARSTVI, (1999 Apr) 45 (4) 238-42. Ref: 38

Journal code: 0413602. ISSN: 0042-773X.

PUB. COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: Czech

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200011

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322

Entered Medline: 20001109

AB Several cytokines stimulating hematopoiesis, mainly lineage restricted, are already widely used in supportive care to correct myelosuppression or anaemia (GM-CSF, G-CSF, EPO). The new growth factor are tested in

preclinical or clinical studies to abrogate other anti-cancer therapy side-effects (thrombocytopenia, mucositis etc.). IL-3 has been shown to have only limited effect on neutrophils and platelets production respectively. IL-6 and IL-11 have been tested to improve thrombocytopenia and mucositis (IL-11). Thrombopoietin (TPO, c-mpl) is tested in clinical trials and shows very strong effect on platelet counts. Stem cell factor (SCF) has shown to improve progenitor cell mobilisation, particularly in combination with other cytokines. The new promising factor, FLT-3 ligand, combines effect on hematopoiesis with effect on dendritic cells generation. The new group of synthetic cytokines (daniplestim, myelopoetin, promegapoetin and progenipoetin) is now tested in preclinical and clinical studies. Mucositis could be influenced by new keratinocyte growth factor (KGF), which is now in phase I trials.

L6 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 12
 ACCESSION NUMBER: 1998:583825 CAPLUS
 TITLE: The therapeutic utility of Interleukin-11 in the

treatment of inflammatory disease
 AUTHOR(S): Trepicchio, William L.; Dörner, Andrew J.
 CORPORATE SOURCE: Department of Preclinical Molecular and Cellular Biology, Genetics Institute, Andover, MA, 01810, USA
 SOURCE: Expert Opin. Invest. Drugs (1998), 7(9), 1501-1504

CODEN: EOIDER; ISSN: 1354-3784
 PUBLISHER: Ashley Publications
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Interleukin-11 (IL-11) is a pleiotropic cytokine that exhibits anti-inflammatory and mucosal protective effects in a variety of animal models of acute and chronic inflammation, such as mucositis, inflammatory bowel disease and autoimmune joint disease. This redn. in inflammation and epithelial damage is mediated in part through effects of recombinant human (rh) IL-11 on macrophage effector function and epithelial cell growth. In vitro studies indicate that rhIL-11 inhibits tumor necrosis factor (TNF)-alpha., IL-1.beta., IL-12, IL-6, and nitric oxide prodn. from activated macrophages. Anal. of the effects of rhIL-11 on transcription factors that activate pro-inflammatory cytokines demonstrate that the level of induced nuclear factor kappa B (NF-kappa.B) binding activity in the nucleus of rhIL-11-treated peritoneal macrophages is significantly reduced. Studies of normal intestinal epithelial cells

indicate that rhIL-11 reduces the rate of cellular proliferation. Anal. of cell-cycle progression demonstrates that growth inhibition of epithelial cells by rhIL-11 correlates with delayed entry into S phase and suppression of pRB phosphorylation. IL-11 also protects intestinal crypt stem cells from radiation- or chemotherapy-induced insults. Such immunomodulatory and epithelial activities may contribute to the protective effects of this cytokine and support the clin. utility of rhIL-11 in the treatment of mucositis, as well as a variety of chronic inflammatory diseases, such as Crohn's disease and rheumatoid arthritis.

L6 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:406367 CAPLUS
 DOCUMENT NUMBER: 129:80275
 TITLE: Acceleration of recovery of small intestinal mucosal

cells by IL-11
 AUTHOR(S): Teramura, Masanao
 CORPORATE SOURCE: Dep. Hematol., Tokyo Women's Med. Coll., Tokyo, 162, Japan
 SOURCE: Ensho to Men'eki (1998), 6(4), 441-445

CODEN: ENMEFA; ISSN: 0918-8371
 PUBLISHER: Sentan Igakusha
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: Japanese
 AB A review with 12 refs. discussing the effects of IL-11 on the recovery of small intestinal mucosal cells that have been damaged by chemotherapy, radiation, short bowel syndrome, colitis, burning, and chemotherapy-induced mucositis.

L6 ANSWER 19 OF 27 MEDLINE
 DUPLICATE 13
 ACCESSION NUMBER: 97392673 MEDLINE
 DOCUMENT NUMBER: 97392673 PubMed ID: 9245489
 TITLE: Mitigating effects of interleukin 11 on consecutive courses of 5-fluorouracil-induced ulcerative mucositis in hamsters.
 AUTHOR: Sonis S T; Van Vugt A G; McDonald J; Dotoli E;
 Schwertschlag U; Szkut P; Keith J
 CORPORATE SOURCE: Division of Oral Medicine Oral and Maxillofacial Surgery, and Dentistry, Brigham & Women's Hospital, Boston, MA 02115, USA.
 SOURCE: CYTOKINE, (1997 Aug) 9 (8) 605-12.

Journal code: 9005353. ISSN: 1043-4666.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199710
 ENTRY DATE: Entered STN: 19971024

Last Updated on STN: 19971024

Entered Medline: 19971014

AB Ulcerative mucositis is a painful, debilitating and dose-limiting toxicity of cancer chemotherapy. Current treatment is largely palliative and no adequate preventive treatment exists. Recently, we reported that recombinant human(rh) interleukin 11 (IL-11) favourably modified the course of mucositis following a single stomatotoxic regimen of 5-fluorouracil in hamsters. Although potentially beneficial, the clinically relevant issue of mucositis and myelosuppression during multicourse chemotherapy treatment was not addressed. The present study was undertaken to evaluate the effect of rhIL-11 on two consecutive courses of mucositis and myelosuppression in hamsters. Ulcerative mucositis was induced using a standardized protocol consisting of 5-fluorouracil (60 mg/kg) on days 1 and 2 followed by superficial irritation of the buccal mucosa on day 4. Animals treated with 100 microg of rhIL-11 for 12 consecutive days following each regimen of chemotherapy experienced a reduction in the incidence, severity, and duration of mucositis, a reduction in weight loss, and less morbidity and mortality relative to control animals. Bone marrow cellularity and function was not adversely affected by rhIL-11 treatment. The present study is consistent with the potential use of rhIL-11 treating patients at risk of developing ulcerative mucositis while undergoing intensive multicourse chemotherapy treatment.

L6 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2002
ACS DUPLICATE 14
ACCESSION NUMBER: 1998:371037 CAPLUS
DOCUMENT NUMBER: 129:134807
TITLE: Interleukin-11: biological activity and clinical studies

AUTHOR(S): Dorner, Andrew J.; Goldman, Samuel J.; Keith, James C., Jr.

CORPORATE SOURCE: Department of Preclinical Research and Development, Genetics Institute Inc., Cambridge, MA, USA

SOURCE: BioDrugs (1997), 8(6), 418-429
CODEN: BIDRF4; ISSN: 1173-8804

PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 64 refs. Interleukin-11 (IL-11) is a cytokine which interacts with a variety of hemopoietic and non-hemopoietic cell types. Recombinant human IL-11 (rhIL-11; oprelvekin) is produced in *E. coli* and differs from the

naturally occurring protein only in the absence of the N-terminal proline

residue. In synergy with other factors, rhIL-11 stimulates the growth of myeloid, erythroid, and megakaryocyte progenitors in vitro. In vivo, rhIL-11 is active in mice, rats, dogs, guinea pigs, hamsters, and non-human primates, where the principal activity measured was stimulation of megakaryocytopoiesis and thrombopoiesis. RhIL-11 has shown benefit in 2 clin. trials by reducing severe chemotherapy-induced thrombocytopenia.

In addn. to its thrombopoietic activity, rhIL-11 has also shown activity in models of acute gastrointestinal mucosal damage. RhIL-11 enhanced survival in mice following cytoablative therapy and in a hamster model of chemotherapy-induced oral mucositis, where treatment with rhIL-11 was assocd. with decreased mucosal damage, accelerated healing, and reduced nos. of deaths. RhIL-11 is currently in clin. trials for the treatment of chemotherapy-induced mucositis. In rat models of acute colonic injury and inflammatory bowel disease, rhIL-11 treatment reduced intestinal mucosal damage and alleviated clin. signs. RhIL-11 has direct effects on activated macrophages to reduce the prodn. of pro-inflammatory mediators. In animal models of endotoxemia, rhIL-11 treatment reduced serum levels of pro-inflammatory cytokines and blocked hypotension. RhIL-11 increased survival in models of Gram-neg. sepsis and toxic shock. Mechanistically, rhIL-11 functions at many levels to control inflammation, ameliorate tissue damage, and maintain hemostasis in the face of trauma or infection. RhIL-11 has direct effects on hepatocytes, inducing the prodn. of acute phase reactant proteins, heme oxygenase, and TIMP-1. RhIL-11 administration has been assocd. with increased plasma levels of von Willebrand factor and fibrinogen. RhIL-11 treatment potentially offers multiple benefits for cancer chemotherapy, such as prevention of thrombocytopenia, gastrointestinal epithelial protection, and subsequent redn. of mucositis, and amelioration of inflammatory complications.

L6 ANSWER 21 OF 27 MEDLINE
DUPLICATE 15
ACCESSION NUMBER: 2000453978 MEDLINE
DOCUMENT NUMBER: 20464824 PubMed ID: 11012229
TITLE: The clinical development of recombinant human interleukin 11 (NEUMEGA rhIL-11 growth factor).
AUTHOR: Kaye J A

CORPORATE SOURCE: Clinical Research/Hematology, Genetics Institute, Inc., Cambridge, Massachusetts 02140, USA.

SOURCE: STEM CELLS, (1996) 14 Suppl 1 256-60. Ref: 26
Journal code: 9304532. ISSN: 1066-5099.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200011

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001102

AB Completed phase I and II studies of recombinant human interleukin 11 (rhIL-11) demonstrate its potential as a treatment for chemotherapy-induced thrombocytopenia. In a phase I study, 16 women with breast cancer received rhIL-11 (10, 25, 50, 75 or 100 microg/kg s.c. once daily) before and during cycles of moderately dose-intensive chemotherapy. Platelet counts increased in all patients before chemotherapy. During chemotherapy, the mean platelet count nadirs were 67,000 cells/microl (rhIL-11 10 microg/kg) and greater than 150,000 cells/microl (25, 50 and 75 microg/kg). Thus, doses of 25 microg/kg and higher appeared to prevent chemotherapy-induced thrombocytopenia in this study. In a randomized, placebo-controlled study, rhIL-11 (50 microg/kg) prevented the need for platelet transfusions during a subsequent chemotherapy cycle in patients who had already experienced severe chemotherapy-induced thrombocytopenia. Among 82 evaluable patients, 8 (30%) of 27 patients administered rhIL-11 50 microg/kg avoided platelet transfusions versus one (4%) of 28 who received placebo ($p < 0.05$). rhIL-11-treated patients received approximately two-thirds the number of platelet transfusions that placebo-treated patients received. The median duration of thrombocytopenia ($<50,000$ cells/microl) was seven days in rhIL-11-treated patients compared to 10 days among patients given placebo. This is the first study in which patients with a history of severe chemotherapy-induced thrombocytopenia who were receiving a variety of chemotherapy regimens have been shown to avoid platelet transfusions following the administration of a thrombopoietic growth factor. This activity of rhIL-11, and the demonstration in preclinical models that it ameliorates chemotherapy-induced mucositis, have promoted its further

clinical development as a supportive therapy in patients receiving chemotherapy.

L6 ANSWER 22 OF 27 MEDLINE
DUPLICATE 16
ACCESSION NUMBER: 1998039347 MEDLINE
DOCUMENT NUMBER: 98039347 PubMed ID: 9372078
TITLE: Clinical development of recombinant human interleukin-11 to treat chemotherapy-induced thrombocytopenia.
AUTHOR: Kaye J A
CORPORATE SOURCE: Genetics Institute, Cambridge, MA 02140, USA.
SOURCE: CURRENT OPINION IN HEMATOLOGY, (1996 May) 3 (3) 209-15.
Ref: 55
Journal code: 9430802. ISSN: 1065-6251.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199712

ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971209

AB Recombinant human interleukin-11 stimulates megakaryocytopoiesis in vitro and platelet production in vivo. A clinical program to investigate the use of recombinant human interleukin-11 in patients with chemotherapy-induced thrombocytopenia began in 1992. These studies show the potential of recombinant human interleukin-11 as a treatment for chemotherapy-induced thrombocytopenia. The other activities of recombinant human interleukin-11, such as its ability to ameliorate mucositis in myelosuppressed animal models, may contribute to its clinical benefits in patients receiving chemotherapy.

L6 ANSWER 23 OF 27 CANCERLIT
ACCESSION NUMBER: 96625162 CANCERLIT
DOCUMENT NUMBER: 96625162
TITLE: Interleukin-11: a new thrombopoietic agent (Meeting abstract).
AUTHOR: Gordon M S
CORPORATE SOURCE: Indiana Univ. Medical Center, Indianapolis, IN.
SOURCE: Non-serial, (1995) 3rd International Conference: Clinical Applications of Cytokines and Growth Factors in Hematology and Oncology, June 8-10, 1995, Atlanta, GA, p. 31, 1995. .
DOCUMENT TYPE: (MEETING ABSTRACTS)
(CLINICAL TRIAL)
(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Institute for Cell and Developmental Biology

ENTRY MONTH: 199606

ENTRY DATE: Entered STN: 19960911

Last Updated on STN: 19960911

AB Interleukin-11 is a hematopoietic growth factor in the

GP130 family of cytokines. In vitro it is synergistic with other cytokines such as IL-3 and c-kit ligand for the proliferation of early hematopoietic progenitors. In pre-clinical studies, IL-11 induces an increase in the number of platelets and reduces the depth and duration of post-chemotherapy thrombocytopenia in a variety of models. It has also been noted that IL-11 has the ability to decrease the development of mucositis in a murine model. IL-11 has been well tolerated in Phase I clinical trials with side

effects comprised primarily of arthralgias and myalgias at doses greater than 50 ug/kg. While all patients experience a therapy-related anemia, no fevers or capillary leak syndrome was seen.

Treatment with IL-

11 at doses ranging from 10-75 ug/kg results in a dose-related increase in platelet counts. Treatment with IL-11 at doses of 25 ug/kg and higher resulted in less thrombocytopenia as compared to patients treated at the 10 ug/kg dose level. Phase I studies in the

setting of bone marrow transplantation have demonstrated a similar safety profile. A recently completed randomized, placebo-controlled phase II

trial of IL-11 has demonstrated a reduction in the incidence of platelet transfusion in patients receiving dose-intensive

chemotherapy. This improvement was especially significant for patients receiving IL-11 at a dose of 50 ug/kg. The side effect profile was similar to that seen in the phase I trials including anemia, mild constitutional complaints, and symptoms related to fluid retention.

IL-11 is a new thrombopoietic agent with the potential

to impact upon chemotherapy-induced thrombocytopenia.

L6 ANSWER 24 OF 27 CANCERLIT

ACCESSION NUMBER: 95609965 CANCERLIT

DOCUMENT NUMBER: 95609965

TITLE: Effect of topical and subcutaneous administration of

interleukin-11 on chemotherapy-induced ulcerative mucositis in hamsters (Meeting abstract).

AUTHOR: Sonis S T; Dotoli E A; Muska A D; Van Vugt A G; Keith J C

CORPORATE SOURCE: Harvard School of Dental Medicine, Boston, MA, 02115.

SOURCE: Proc Annu Meet Am Assoc Cancer Res, (1995) 36 A2190.

ISSN: 0197-016X.

DOCUMENT TYPE: (MEETING ABSTRACTS)

LANGUAGE: English

FILE SEGMENT: Institute for Cell and Developmental Biology

ENTRY MONTH: 199508

ENTRY DATE: Entered STN: 19950809

Last Updated on STN: 19950809

AB The purpose of this study was to determine the effect of topically applied

interleukin-11 (IL-11, Genetics Institute, MA) on the course of ulcerative mucositis (UM), a

painful, debilitating and dose-limiting side effect of cancer chemotherapy, and to evaluate the effect of varying regimens of IL

-11. 95 male golden Syrian hamsters were equally divided into 5

groups (G). G1 (control) received phosphate buffered saline and 0.5%

autologous hamster serum (vehicle) topically on days (d) 3-14. G2 and 4

were given 50 ug of IL-11 sc, bid, on d 0-14 and 3-14,

respectively. 100 ug of IL-11 was administered qid topically on d 3-14 to G3, and d 0-14 to G5. To

induce UM, animals received 60 mg/kg of 5-fluorouracil on d 0 and 2.

The left buccal pouch

was superficially irritated on d 4. UM was evaluated blindly starting on d

6 by scoring standardized photographs (scale 0-10, 10 most severe).

Animals were weighed daily. Blood was taken from 3 animals per group on d

6, 10, and 14. For the entire experiment, the average mean UM scores for

all groups (G2 = 3.8, G3 = 4.1, G4 = 3.3 and G5 = 4.0) was significantly

(t-test, p less than 0.05) lower than the control (5.0). In comparing mean

UM scores by day, sc administration of IL-11 was more

efficacious than topically applied IL-11 from d 6-9.

Although not significant, G4 demonstrated mean UM scores lower than G2 for

d 9-12. This finding suggests a possible advantage to administering

IL-11 after chemotherapy. G4 had significantly higher

average % weight gain compared to G1 (d 3 and 5-8), G3 (d 6-9), and G5 (d

1-8). Significant weight loss was observed in G4 compared to G2 on d 1-3,

5, 9, and 10. On d 10, significantly higher mean platelet counts (K/uL)

were demonstrated by G2, 4, and 5, achieving values of 49.0%, 105.5%, and

87.8% greater than the control. The 14-d survival rates for G1-5 were 23%,

69%, 38%, 100% and 46%. While both sc and topical administration of

IL-11 favorably modified the course of chemotherapy-induced UM, IL-11 given sc, d 3-14, was

the most efficacious regimen.

L6 ANSWER 25 OF 27 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1995:186374 BIOSIS

DOCUMENT NUMBER: PREV199598200674

TITLE: Effect of topical and subcutaneous administration of

interleukin-11 on chemotherapy-induced ulcerative mucositis in hamsters.

AUTHOR(S): Sonis, S. T. (1); Dotoli, E. A.;
Muska, A. D.; Van Vugt, A.
G.; Keith, J. C.
CORPORATE SOURCE: (1) Harvard Sch. Dent.
Med., Boston, MA 02115 USA
SOURCE: Proceedings of the American
Association for Cancer Research
Annual Meeting, (1995) Vol. 36, No. 0, pp.
368.
Meeting Info.: Eighty-sixth Annual Meeting
of the American
Association for Cancer Research Toronto,
Ontario, Canada
March 18-22, 1995
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 26 OF 27 MEDLINE
DUPLICATE 17
ACCESSION NUMBER: 96103636 MEDLINE
DOCUMENT NUMBER: 96103636 PubMed ID:
7492924
TITLE: Alteration in the frequency, severity and
duration of
chemotherapy-induced mucositis in
hamsters by
interleukin-11.
AUTHOR: Sonis S; Muska A; O'Brien J; Van
Vugt A; Langer-Safer P;
Keith J
CORPORATE SOURCE: Division of Oral Medicine
and Dentistry, Brigham and
Women's Hospital, Boston,
Massachusetts, USA.
SOURCE: EUROPEAN JOURNAL OF
CANCER. PART B, ORAL ONCOLOGY, (1995
Jul) 31B (4) 261-6.
Journal code: 9214373. ISSN: 0964-1955.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL
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AB Ninety-five young, male Golden Syrian hamsters
were randomly divided into
five equally sized groups. One group served as a
placebo control while the
animals in the others received one of four doses of
interleukin-eleven (IL-11) twice daily given by subcutaneous injection
beginning on the first day of chemotherapy (day 0)
and continuing to day
14. Mucositis was induced with 5-fluorouracil using a
standard
regimen of 60 mg/kg, intraperitoneally on days 0 and
2 followed by
superficial mucosal irritation on day 4. Animals were
evaluated daily
beginning on day 6. Mucositis was assessed using a
standardised
technique in which randomly numbered daily
mucosal photographs were scored
by three blinded independent observers at the
conclusion of the
experiment. IL-11 favourably affected the frequency,

severity and duration of mucositis. This
phenomenon appeared to
be dose dependent. Hamsters receiving 30 and 100
micrograms per day of
IL-11 demonstrated significantly ($P < 0.05$) lower
mucositis scores than did either the control or
animals receiving
3 or 10 micrograms per day, although the latter had
marginal beneficial
effects. Additionally, survival was significantly better
for hamsters
receiving higher doses of IL-11 (85%) compared to
the
placebo control (46%). IL-11 administration also
favourably affected weight loss. While stimulation of
platelet production
was noted in animals receiving IL-11, a lack of
difference in bone marrow cellularity between test
and control animals
suggests that the mechanism by which IL-11
modifies
mucositis is mediated at the epithelial or connective
tissue level
rather than through the marrow. The kinetics of IL-11
alteration of mucositis induction supports such a
hypothesis.
Further investigation is currently underway to
establish a definitive
mechanism by which IL-11 protects the oral mucosa.

L6 ANSWER 27 OF 27 MEDLINE
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ACCESSION NUMBER: 95211031 MEDLINE
DOCUMENT NUMBER: 95211031 PubMed ID:
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TITLE: IL-11, a pleiotropic cytokine: exciting
new effects of
IL-11 on gastrointestinal mucosal biology.
AUTHOR: Keith J C Jr; Albert L; Sonis S T;
Pfeiffer C J; Schaub R G
CORPORATE SOURCE: Genetics Institute, Inc.,
Cambridge, Massachusetts.
SOURCE: STEM CELLS, (1994) 12 Suppl 1 79-
89; discussion 89-90.
Journal code: 9304532. ISSN: 1066-5099.
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AB Recombinant human interleukin 11 (rhIL-11) is a
pleiotropic cytokine that stimulates bone marrow
stem cells to proliferate
and decreases intestinal mucosal injury produced by
cytoablative drugs and
radiation in animals. The effects of rhIL-11 were
studied in a hamster
model of oral mucositis and in two rat models of
inflammatory
bowel disease (IBD). Oral mucositis was induced in
male Golden
Syrian hamsters with 5-fluorouracil 60 mg/kg
intraperitoneal, days 0 and
2. Peak mucositis occurred by day 10 in vehicle
treated animals.

rhIL-11, given twice daily subcutaneously,
decreased the mucositis
in a dose-dependent manner and increased animal
survival at all doses
tested. In two models of IBD, the acetic acid-induced
acute colonic injury
model in Sprague-Dawley rats and the transgenic
Fischer 344 rats
expressing human HLA-B27 and beta 2-
microglobulin, rhIL-11 decreased the
gross and microscopic damage in the colons of
these animals. These data
suggest that rhIL-11 exerts effects on the
gastrointestinal mucosa which
ameliorate responses to injurious stimuli.

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